CLAIMS AMENDMENT

What is claimed is:

(*please substitute the following claim 1 for the pending claim one*)

1. "three times amended"

The use of thiophosphate for synthesizing phosphorothioate substituted nucleic acids in vivo by

1) preparing microbial culture media depleted of phosphate
2) adding thio-phosphate as an alternative source of phosphate to the media
3) culturing micro-organisms in the modified media containing thiophosphate to allow the uptake and incorporation of thiophosphate into nucleotide precursor pools thereby leading to the synthesis of phosphorothioate internucleotide linkages in vivo.

(*please substitute the following claim 2 for the pending claim two*)

2. "amended"

The method of claim 1 used to generate phosphorothioate recombinant plasmid DNA, recombinant phage DNA including single-stranded M13 phage DNA, or RNA produced from a recombinant viral or plasmid vector by

1) transforming bacterial cultures with the desired recombinant DNA plasmid or recombinant DNA phage

2) growing the transformed cultures in modified media containing thiophosphate as a source of phosphate

3) isolating the recombinant plasmid DNA, phage DNA, or RNA produced by a recombinant vector from said bacterial cultures.

(*please substitute the following claim 3 for the pending claim three*)

3. "twice amended"

The method of claim 1 used to generate partially substituted phosphorothioate recombinant plasmid DNA, recombinant phage DNA, including single-stranded M13 phage DNA, or RNA produced from a recombinant viral or plasmid vector by

1) transforming bacterial cultures with the desired recombinant DNA plasmid or recombinant DNA phage

2) growing the transformed cultures in modified media containing a mixture of thiophosphate and unmodified phosphate as a source of phosphate

3) isolating the recombinant plasmid DNA, phage DNA, or RNA produced by a recombinant vector from said bacterial cultures.

4. "twice amended"

The method of claim 1 wherein the cells cultured in thio-phosphate media or induced to uptake thio-phosphate are of eukaryotic origin.

(*please substitute the following claim five for the pending claim five*)

5. "three times amended"

The method of claim 1 where the alternative source of phosphate is a derivative of thiophosphate including but not limited to dithiophosphate and/or methylthiophosphate.

CLAIMS AMENDMENT

(Marked Up Version)

What is claimed is:

1. "three times amended"

~~A process for generating~~ The use of thiophosphate for synthesizing phosphorothioate substituted nucleic acids in vivo ~~comprising~~ by

1) preparing microbial culture media depleted of phosphate
2) adding thio-phosphate as an alternative source of phosphate to the media
3) culturing micro-organisms in the modified media containing thiophosphate ~~such that~~ to allow the uptake and incorporation of thiophosphate into nucleotide precursor pools thereby ~~enabling~~ leading to the synthesis of phosphorothioate internucleotide linkages in vivo.

2. "amended"

The method of claim 1 used to generate phosphorothioate ~~ds DNA, ssDNA, and/or RNA~~ recombinant plasmid DNA, recombinant phage DNA, including single-stranded M13 phage DNA, or RNA produced from a recombinant viral or plasmid vector by ~~the in vivo incorporation of thio-phosphate into nucleotide precursor pools.~~

1) transforming bacterial cultures with the desired recombinant DNA plasmid or recombinant DNA phage

2) growing the transformed cultures in modified media containing thiophosphate as a source of phosphate

3) isolating the recombinant plasmid DNA, phage DNA, or RNA produced by a recombinant vector from said bacterial cultures.

3. "twice amended"

The method of claim 1 used to generate ~~ds DNA, ssDNA, or RNA~~ partially substituted ~~with~~ phosphorothioate ~~linkages~~ recombinant plasmid DNA, recombinant phage DNA including single-stranded M13 phage DNA, or RNA produced from a recombinant viral or plasmid vector by ~~the in vivo incorporation of thio-phosphate into nucleotide precursor pools.~~

1) transforming bacterial cultures with the desired recombinant DNA plasmid or recombinant DNA phage

2) growing the transformed cultures in modified media containing a mixture of thiophosphate and unmodified phosphate as a source of phosphate

3) isolating the recombinant plasmid DNA, phage DNA, or RNA produced by a recombinant vector from said bacterial cultures.

4. "twice amended"

The method of claim 1 wherein the cells cultured in thio-phosphate media or induced to uptake thio-phosphate are of eukaryotic origin.

5. "three times amended"

The method of claim 1 where the alternative source of phosphate is a derivative of thiophosphate ~~such that~~ including but not limited to dithiophosphate and/or methylthiophosphate.